Citation:

Kristensen M, Jensen M, Kudsk J, Henriksen M, Mølgaard C. Short-term effects on bone turnover of replacing milk with cola beverages: a 10-day interventional study in young men. *Osteoporos Int.* 2005 Dec;16(12):1803-8.

PubMed ID: 15886860

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To investigate the short-term effects of replacing milk with cola beverages in young men on a low-calcium diet in order to study the effects of this replacement on calcium homeostasis and bone turnover.

Inclusion Criteria:

- Healthy Caucasian males aged 22-29 years
- All university students

Exclusion Criteria:

- Smokers
- Elite athletes (>10h/week)
- Students who have taken dietary supplements or donated blood three months prior to the study

Description of Study Protocol:

Recruitment : Young men were recruited at the university.

Design: Randomized crossover trial

Blinding used (if applicable): not mentioned

Intervention (if applicable):

- 2.5 liter of Coca Cola or semi-skimmed milk per day in a two 10-day experimental periods with an intervening 10-day washout period.

- During the two periods the same low-calcium basic diet was given to the subjects.

Statistical Analysis:

- Data were controlled for homogeneity of variance verified by residual plots, and the changes from baseline to end point were analyzed by paired *t*-test.
- Mixed model analysis was performed using the MIXED procedure. When the effect of treatment was evaluated, end point concentrations of the biochemical markers were modeled as the dependent variable.
- The statistical significance was defined as $p<0.05$.

Data Collection Summary:

Timing of Measurements: Biochemical markers were measured at baseline and on the last day of each intervention period of ten days.

Dependent Variables

- Calcium
- Phosphate
- 1,25(OH)2D
- PTH
- Osteocalcin
- B-ALP (bone specific alkaline phosphatase)
- CTX (cross-linked C-telopeptides)
- NTX (cross-linked N-telopeptides)

Independent Variables

- Milk 2.5 L- subjects were instructed to consume a minimum of 1.5 L of semi-skimmed milk in combination with the meals. The average intake of calcium was 3,100mg calcium per day and the energy derived from protein was 20.2%.
- Cola 2.5 L - same procedure. The energy intake provided in the cola was the same as in the milk. However, the energy derived from protein was only 9.4% and calcium intake was 1,690mg per day.
- Two different lunch meals and three different dinner meals were served in the same order during the two intervention periods. All the meal but dinner were served in the institute. However, the food and drinks for the dinner were given by the researchers to be consumed at home.

Control Variables

Description of Actual Data Sample:

Initial N: 11 males

Attrition (final N): 11 males

Age: 22-29 years

Ethnicity: Caucasian

Other relevant demographics:

Anthropometrics:

Location: Frederiksberg, Denmark

Summary of Results:

Key Findings

- An increase in serum phosphate ($P < 0.001$), $1,25(OH)_2D$ ($P < 0.001$), PTH ($P = 0.046$) and osteocalcin ($P < 0.001$) was observed in the cola period compared to the milk period.
- Also, bone resorption was significantly increased following the cola period, seen as increased serum CTX ($P < 0.001$) and urinary NTX ($P < 0.001$) compared to the milk period.
- No changes were observed in serum concentrations of calcium or B-ALP.
- Calcium serum concentration did not show difference between the two treatments but a treatment by period interaction was seen ($p=0.002$)
- After cola treatment there was a significantly increase in the PTH ($p<0.02$), Osteocalcin ($p<0.014$) and $1,25(OH)_2D$, $p<0.019$ when compared to the baseline.

Author Conclusion:

This study demonstrates that over a 10-day period high intake of cola with a low-calcium diet induces increased bone turnover compared to a high intake of milk with a low-calcium diet. Thus, the trend towards a replacement of milk with cola and other soft drinks, which results in a low calcium intake, may negatively affect bone health as indicated by this short term study.

Reviewer Comments:

- *The small sample size increases the possibility of type 2 error and may not determine whether consumption of cola replacement induces increased bone turnover*
- *Authors recognize that no conclusions can be taken on the effect of cola because neither a non-cola carbonated beverage nor a cola and high-calcium diet period were included.*
- *In the milk period the energy derived from protein was higher compared to the cola which may have a short-term calciuric effect.*
- *Interventions lasted only 10 days each*
- *Finally the results are limited to a young male population.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes

2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	N/A
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	No
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	???

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	???
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	???
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes